Orphan Drug Development Guidebook

Building Block E118

This document defines the content of the Building Block created for each identified tool, incentives, initiative or practice introduced by public bodies or used by developers to expedite drug development in Rare Diseases (RDs).

ITEM	DESCRIPTION
Building Block (BB) Title	Centralised EMA Marketing Authorisation (MA) with post-authorisation studies and measures
References	Post authorisation safety studies (PASS) https://www.ema.europa.eu/en/human-regulatory/post-authorisation/pharmacovigilance/post-authorisation-safety-studies-pass-0 Post authorisation efficacy studies (PAES) https://www.ema.europa.eu/en/human-regulatory/post-authorisation/post-authorisation-efficacy-studies-questions-answers Post authorisation measures (PAM) https://www.ema.europa.eu/en/human-regulatory/post-authorisation/post-authorisation-procedural-qa/post-authorisation-measures-questions-answers
Description	A marketing authorisation may be granted with certain conditions in order to ensure the collection of additional safety and or efficacy data. A post-authorisation safety study (PASS) is any study relating to an authorised medicinal product conducted with the aim of identifying, characterizing or quantifying a safety hazard, confirming the safety profile of the medicinal product, or of measuring the effectiveness of risk management measures. Post-authorisation efficacy studies (PAES) may be imposed at the time of the grant of the initial MA where concerns relating to some aspects of the efficacy of the medicinal product are identified and can be resolved only after the medicinal product has been marketed. Smaller studies are more susceptible to the effects of variability, and missing data is more likely to have a greater impact on the study conclusions. Smaller pre-marketing exposure in rare diseases often equates with the increased importance of and emphasis on post-market monitoring and data collection. Duration depends on the nature of the studies and the issues to be resolved.

Category	Regulatory Building Block
Geographical scope	European Union
Availability	Applicants developing medicines for rare and non-rare diseases. However, MA with conditions is more likely to involve rare disease research where there are gaps in the knowledge base due to the small population research challenges.
Scope of use	PAES and PASS are imposed at the time of the marketing authorisation by the EMA's CHMP. May be a topic for scientific advice discussion. Potential requirement to gain a marketing authorization.
Stakeholders	• EMA's CHMP • Holders of registries
Enablers/ Requirements	Requirement for PAES / PASS should be proactively considered by the drug developer when determining what might be the gaps for any regulatory submission.
Output	Mandated collection of additional data post authorisation
Best time to apply and time window	Imposed by the CHMP at the time of MA. However, it is important to proactively consider it during the development program and as a potential topic for a scientific advice question to regulatory authorities.
Expert tips	Actively consider post authorisation requirements as part of the pre-submission dossier submission to promote a smoother regulatory review. PROs: • Approval with conditions is a regulatory licensing flexibility that allows approval whilst ensuring the collection of additional data to support the benefit risk conclusions CONs:

	• Additional expenses for running new studies, registries, etc